ABSTRACT

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Title of diploma thesis: Interaction of natural substances with human aldo-keto reductase 7A2 and other important carbonyl reducing enzymes

Reduction of carbonyl group is one of the phase I metabolism reactions, which is responsible for production of more polar metabolites, enables conjugation in process of biotransformation, excretion of the molecule and it also causes decrease in reactivity and biological activity of the molecule. Endogenous as well as exogenous compounds undergo this reaction and carbonyl reducing enzymes are the ones which possess this reducing activity. Based on the structure, we can divide the enzymes into several groups: short-chain dehydrogenases/reductases, medium-chain dehydrogenases/reductases, aldo-keto reductases and quinone reductases. Inhibition of carbonyl reducing enzymes appears to be a promising aim of research. It is important to take into consideration that by inhibiting carbonyl reducing enzymes it is possible to reduce production of less active, but more toxic metabolites, for example in anthracycline chemoteraputics daunorubicin and doxorubicin and that can lead to change in therapy of cancer.

This study focused on determination of inhibition activity of natural compounds from flavonoid and alkaloid structural groups. The reducing reaction of anticancer drug daunorubicin to its more toxic metabolite daunorubicinol was used to compare the inhibiting activity. To analyse the results, UHPLC analysis was performed and the IC_{50} was established for the most significant inhibitor.